APPENDIX A

Art Unit 1804 MAILED Paper No. 16

Appeal No. 91-0967 NOV 26 1991 cag

ON BRIEF BOARD OF PATENT APPEALS AND INTERFERENCES

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte David A. Fischhoff
and Stephen G. Rogers

Application for Patent filed November 20, 1986, Serial No. 06/932,818. Insect-Resistant Tomato Plants.

Thomas P. McBride et al. for appellants.

Supervisory Patent Examiner - Charles F. Warren.
Examiner - Charles E. Cohen.

Before Pellman, Goolkasian and W. Smith, Examiners-in-Chief.

W. Smith, Examiner-in-Chief.

This is an appeal from the final rejection of claims 1 through 9 and 37, all the claims in the application.

Claim 1 is illustrative of the subject matter on appeal and reads as follows:

1. A method of producing genetically transformed tomato plants which exhibit toxicity toward Lepidopteran larvae which comprises:

(a) inserting into the genome of a tomato cell a chimeric gene which comprises

(i) a promoter which functions in plants to cause the production of a mRNA transcript;

(ii) a coding sequence that causes the production of mRNA encoding a crystal protein toxin of *Bacillus thuringiensis*; and

(iii) a 3′ non-translated region which functions in tomato to cause the addition of polyadenylate nucleotides to the 3′ end of the mRNA;

(b) selecting transformed tomato cells; and

(c) regenerating from the transformed tomato cells genetically transformed tomato plants which exhibit toxicity toward Lepidopteran larvae.

The references relied upon by the examiner are:

Schnepf et al. (Schnepf)	4,467,036	Aug. 21, 1984
Adang et al. (Adang) (European Patent Application)	142,924	May 29, 1985
Vaeck et al. (Vaeck) (DeGreve) (European Patent Application)	193,259	Sept. 3, 1986

Harding, "Field Comparisons Of Insecticidal Sprays For Control Of Four Tomato Insects In South Texas", *Journal Of Economic Entomology*", Vol. 64, No. 5, pages 1302-1304 (1971).

Wolfenbarger et al. (Wolfenbarger), "Tomato Pinworm Control", *Florida State Horticultural Society*", pages 139-143 (1973).

Caplan et al. (Caplan), "Introduction Of Genetic Material Into Plant Cells", *Science*, Vol. 22, pages 815-821 (1983).

Adang et al., "Characterized Full-Length And Truncated Plasmid Clones Of The Crystal Protein of *Bacillus thuringiensis* subsp. *Kurstaki*-HD-73 And Their Toxicity To *Manduca Secta*", *Gene*, Vol. 36, pages 289-300 (1985) (Adang Gene).

Schnepf et al. (Schnepf), "The Amino Acid Sequence Of A Crystal Protein From *Bacillus thuringiensis* Deduced From The DNA Base Sequence", *The Journal Of Biological Chemistry*, Vol. 260, No. 10, pages 6264-6272 (1985).

Vaeck et al. (Vaeck), "Transgenic Plants Protected From Insect Attack", *Nature*, Vol. 328, pages 33-37 (1987).

Barton et al. (Barton), "*Bacillus thuringiensis* δ-Endotoxin Expressed In Transgenic *Vicotiana tabacum* Provides Resistance To Lepidopteran Insects", *Plant Physiology*, Vol. 85, pages 1103-1109 (1987).

Claims 1, 2, 6, and 37 stand rejected under 35 USC § 112, first paragraph, as being nonenabled and claims 1 through 9 and 37 stand rejected under 35 USC § 103 as unpatentable over DeGreve in view of Caplan, Schnepf '036, Schnepf, and Adang (Gene).

We affirm the rejection under 35 USC § 103 and reverse the rejection under 35 USC § 112, first paragraph.

REJECTION UNDER 35 USC § 112, FIRST PARAGRAPH

The examiner relies upon Barton, Vaeck and DeGreve in support of the *prima facie* case of nonenablement under this section of the statute. Specifically, the examiner questions whether these claims are enabled throughout their scope since the working examples of the present specification are based on the use of a single *B. thuringiensis* crystal protein toxin gene, i.e., HD-1 gene.

The examiner relies upon Barton and Vaeck for their disclosure that the insertion of a *B.t.* toxin gene in tobacco plants may prove to be lethal to the plant. DeGreve is relied upon for its disclosure on pages 3-4 concerning the difficulty of expressing foreign genes of non-plant origin in transformed plants both generally and as specifically applied to the expression of *B.t.* genes.

As set forth in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), the question to be resolved is whether one skilled in the art would be enabled by the present specification to make and use the invention as claimed without "undue experimentation." After consideration of the evidence of record, we agree with appellants that the specification does provide enabling support for the rejected claims.

The relevance of Barton and Vaeck to this issue is minimal since these references are concerned solely with transforming tobacco plants with *B.t.* toxin genes. Barton does set forth in the "Discussion" portion of the reference that expression of the intact toxin was in someway toxic to plant tissue since transformed plants containing the toxin protein soon died. However, Barton puts this observation in perspective by subsequently noting that *B.t.* toxin is very potent, even to the point of some of the transformed plants being resistant to test pests when toxin protein was expressed below detectable levels.

While not expressly stated by the references, it may be that the noted toxicity was due to "too much of a good thing." Just as too much fertilizer may be toxic to a plant, too much *B.t.* may be toxic. In any event, we view the successful transformation of tobacco plants with various *B.t.* toxin genes which resulted in the transformed plants being insect resistant to be more relevant to the present enablement issue.

DeGreve is somewhat more relevant to the present issues since the reference is generic to transforming plants with *B.t.* toxin genes in order to make the plants insect resistant. The examiner has correctly noted that the background portion of this reference does set forth some of the concerns those skilled in the art would have in transforming plants in general with non-plant genes and specifically with *B.t.* toxin genes. However, this background information must be viewed in the context of the successful work reported by the reference. While the working examples of this reference are directed to tobacco plants, the reference discloses in the paragraph bridging pages 26-27 that plants other than those used in the working examples can be transformed with *B.t.* toxin genes including vegetables. This portion of the reference also takes into account the potential of providing *B.t.* toxin genes in the transformed plants in such a manner that they would be fatal to the plant itself, cautioning against such a happenstance.

DeGreve provides clear direction to those skilled in the art as to how to transform a wide variety of plants, including vegetables, with a *B.t.* toxin gene in order to make these plants insect resistant. While some experimentation may be needed in order to transform a particular plant with a particular *B.t.* toxin gene, we do not find that such experimentation would amount to "undue experimentation."

The rejection under 35 USC § 112, first paragraph, is reversed.

REJECTION UNDER 35 USC § 103

We initially note that the dependent claims have not been separately argued. Therefore, these claims shall stand or fall based upon the limitations found in independent claim 1. *In re Burckel*, 592 F.2d 1175, 201 USPQ 67 (CCPA 1979); 37 CFR § 1.192(c)(5).

DeGreve discloses the method of claim 1 on appeal with the single exception of not explicitly stating that the method of producing genetically transformed plants which exhibit toxicity towards Lepidopteran larvae disclosed in that reference is to be used with tomato plants. See page 22, lines 26-31 of the reference for the disclosure of providing a polyadenylation signal in the chimeric gene of the reference as required by claim 1 on appeal.

In view of the above noted statement in DeGreve that the method of this reference may be used to generically transform plants with a *B.t.* toxin gene, including vegetables, we conclude the subject matter of claim 1 on appeal would have been *prima facie* obvious to one of ordinary skill in the art from a consideration of DeGreve alone. The remaining references relied upon by the examiner appear to have been applied in regard to limitations found in certain of the non-argued dependent claims. Thus, in regard to claim 1 on appeal, these additional references may be considered cumulative.[1]

Appellants argue that DeGreve does not disclose that there would be any expectation of successful transformation of tomato plants. We disagree. DeGreve clearly discloses that the method disclosed in that reference which was successfully employed in tobacco plants in the working examples of the reference would be expected to work in a wide variety of other plants including vegetables. Reading the reference as a whole leads us to the conclusion that one of ordinary skill in the art would reasonably expect a successful transformation of tomato plants with a *B.t.* toxin gene in order to create insect resistant

[1] It should be noted that another reference of record relied upon by appellants in their rebuttal of the *prima facie* case, Adang, specifically lists tomato plants as being recommended for protection by *B.t.* toxin via transformation as in the present invention. See Table 2 of the reference.

tomato plants. This is all that is required to reach a conclusion of *prima facie* obviousness. *In re O'Farrell*, 853 F.2d 894, 7 USPQ2d 1673 (Fed. Cir. 1988).

Appellants rely upon the declaration of Dr. Roy L. Fuchs filed under 37 CFR § 1.132 as evidence of nonobviousness. The premise of Dr. Fuchs's declaration is that prior to the present invention, those of ordinary skill in the art considered control of tomato pinworm problematic through use of *B.t.* and that tomato plants transformed in accordance with the present invention provide protection against tomato pinworm. We have carefully considered Dr. Fuchs's declaration but do not find it entitled to sufficient weight to outweigh the evidence of obviousness relied upon by the examiner.

The first portion of the declaration sets forth background material regarding the use of *Bacillus thuringiensis* bacterium to control a variety of pests on plants including tomato pinworms on tomato plants. All of the references relied upon by Dr. Fuchs in this portion of his declaration are based upon very specific, limited field trials of various products. These references do report a mix of results concerning the use of various *B.t.* products in controlling tomato pinworm. However, as pointed out by the examiner, the Wolfenbarger and Harding references do disclose that tomato pinworm can be controlled under appropriate circumstances by *B.t.* products. This is

entirely consistent with the admission made by appellants at page 1, lines 14-17 of the present specification that tomato pinworms were known at the time of the present invention to be susceptible to the action of the protein toxin of *Bacillus thuringiensis* bacteria.

The mixed results reported by these various studies would appear to be explained by Dr. Fuchs's statement at page 3 of his declaration that pinworm larvae worm beneath the leaf epidermis within 24 hours after hatching which provides a very narrow window for topical control by chemical or biological control agents such as *B.t.* strains or preparations. This is confirmed by Wolfenbarger at page 140. See also page 673 of the Poe reference relied upon by Dr. Fuchs where it states pinworm larvae are protected by their habit of feeding within a leaf fold and it is only when the larvae are forced from cover to seek new feeding sites that they are vulnerable to insecticides.

Since it was known at the time of the present invention that (1) tomato pinworms are susceptible to *B.t.* toxin protein and (2) the effectiveness of these products for this purpose depends upon the ability to deliver the product to a site of the plant where the pinworm is feeding, we do not find the results reported in Dr. Fuchs declaration to be unexpected. Transformation of a tomato plant with a *B.t.* toxin gene would expectedly result in providing the expressed *B.t.* toxin within

the tomato plant tissue where it would be more available to the feeding pinworm larvae.

The rejection under 35 USC § 103 is affirmed.

The decision of the examiner is affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR 1.136(a). See the final rule notice, 54 F.R. 29548 (July 13, 1989), 1105 O.G. 5 (August 1, 1989).

AFFIRMED

Irving R. Pellman
Irving R. Pellman
Examiner-in-Chief

John T. Goolkasian
John T. Goolkasian
Examiner-in-Chief

William F. Smith
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BOARD OF PATENT APPEALS AND INTERFERENCES

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APPENDIX B

44. A chimeric gene comprising:

(a) a promoter that functions in plants;

(b) a coding sequence comprising a full length Bacillus thuringiensis crystal protein gene capable of encoding a Bacillus thuringiensis crystal protein of about 130 kD; and

(c) a 3' non-translated region that functions in plants to cause the addition of polyadenylate nucleotides to the 3' end of an mRNA, wherein said promoter causes said Bacillus thuringiensis crystal protein to be expressible in a plant in an amount insecticidal to lepidopteran insects.

45. The chimeric gene of claim 44 wherein said promoter is selected from the group consisting of the CaMV35S and MAS promoters.

46. The chimeric gene of claim 44 wherein said promoter is the CaMV 35S promoter.